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## Intraaortic Balloon Pump: Incidence and Predictors of Complications in the Florence Registry

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### ABSTRACT

**Background:** The intraaortic balloon pump (IABP) is the most commonly used mechanical circulatory support for patients with acute coronary syndromes and cardiogenic shock. Nevertheless, IABP-related complications are still frequent and associated with a poor prognosis.

**Hypothesis:** To prospectively assess the incidence and predictors of complications in patients treated with IABP.

**Methods:** A total of 481 patients treated with IABP were prospectively enrolled in our registry (the Florence Registry). At multivariable logistic regression analysis the following variables were independent predictors for complications (when adjusted for age >75 years, eGFR and time length of IABP support): use of inotropes (OR 2.450,  $P < 0.017$ ), nadir platelet count (1000/ $\mu$ L step; OR 0.990,  $P < 0.001$ ), admission lactate (OR 1.175,  $P = 0.003$ ). Nadir platelet count showed a negative correlation with length of time of IABP implantation ( $r = -0.31$ ;  $P < 0.001$ ). A nadir platelet count cutoff value of less than 120,000 was identified using a receiver operating characteristic (ROC) curve for the development of complications (area under the curve [AUC] 0.70;  $P < 0.001$ ).

**Results:** Complications were observed in the 13.1%, among whom 33 of 63 showed major bleeding. The incidence of complications was higher in patients aged >75 years ( $P = 0.015$ ) and in those who had an IABP implanted for more than 24 hours ( $P = 0.001$ ). Patients with complications showed an in Intensive Cardiac Care Unit (ICCU) mortality higher than patients who did not (44.4% vs 17.2%,  $P < 0.001$ ).

**Conclusions:** In consecutive patients treated with IABP support, the degree of hemodynamic impairment and the decrease in platelet count were independent predictors of complications, whose development was associated with higher in-ICCU mortality.

### Introduction

The intraaortic balloon pump (IABP) is currently the most commonly used mechanical circulatory support for patients with acute coronary syndromes (ACS) and cardiogenic shock (CS).

According to guidelines,<sup>1</sup> IABP implantation is indicated (class I C) in patients with CS and in those with mechanical complications of acute myocardial infarction. However, in the clinical practice, IABP is often implanted also in hemodynamically stable patients at high risk of complications during percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG).<sup>2–6</sup>

In the last decade, IABP technology has made significant progress (sheathless insertion<sup>7</sup> technique, different balloon diameters, optic fiber IABP) to reduce complications and improve patient support. Nevertheless, IABP-related complications are still frequent and associated with a poor prognosis.<sup>6,8,9</sup>

The present investigation was therefore aimed at prospectively assessing the incidence and predictors of complications in 481 patients treated with IABP implantation and consecutively admitted to our Intensive Cardiac Care Unit (ICCU) (the Florence Registry).

### Methods

#### Study Population

From January 1, 2004 to December 31, 2009, 481 patients underwent intraaortic counterpulsation in our ICCU and were prospectively enrolled in the Florence Registry.

All patient data, including demographics, baseline characteristics and admission diagnosis, type and severity of heart disease, data regarding IABP management, including concomitant medications, which were left to the discretion of the treating physician, were stored in a dedicated database.

According to our policy, testing for heparin-induced thrombocytopenia (HIT) was performed on clinical suspicion and whenever thrombocytopenia (a platelet count <150,000) or a 50% or greater reduction in platelet count from baseline developed.

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Major bleeding was defined according to the ACUTY criteria as follows<sup>10</sup>: intracranial or intraocular bleeding; access site hemorrhage requiring intervention,  $\geq 5$ -cm-diameter hematoma, clinically overt blood loss with hemoglobin decrease  $\geq 3$  g/dL, any hemoglobin decrease  $\geq 4$  g/dL, or blood-product transfusion

## Definitions

**IABP Positioning:** The balloon catheter was inserted according to the Seldinger technique via the left or right femoral artery either in the catheterization laboratory or in the ICCU. Sheathless or non-sheathless insertion was decided according to the operator's discretion. Balloon diameters ranged from 7 to 8 F according to the patient's height. Our ICCU policy is to remove the device as soon as possible, immediately after hemodynamics is restored or at the end of high risk procedures.<sup>6</sup>

**Large Ischemic Risk Area:** The large ischemic risk area (LIRA)<sup>6</sup> was defined as "ejection fraction less than 40% (at angiography or transthoracic echocardiogram) associated with proximal occlusion of left descending anterior coronary artery and or not with coexisting critical lesions in other coronary arteries."

**High-Risk Patients:** Patients were defined as "high risk" if 1 or more of the following criteria were present: left ventricular ejection fraction (LVEF)  $< 40\%$ , Killip class  $\geq 3$ , persistent malignant ventricular arrhythmias, acute mitral regurgitation and severe coronary artery disease (left main stem or 3-vessel or vein graft disease).<sup>6,11</sup>

Informed consent was obtained from all patients.

## Statistical Methods

Patient data were collected and analyzed using SPSS 13.0 statistical software (SPSS Inc., Chicago, IL). Continuous data were tested for normality with the Kolmogorov-Smirnov test; variables that were non-normally distributed were log-transformed in order to meet normality. These variables were expressed as mean  $\pm$  standard deviation (SD) and analyzed by means of Student *t* test. Length of IABP treatment has been reported as median and 25th to 75th percentile; comparisons were made with Mann-Whitney *U* test. Categorical data were reported as frequencies and percentages and analyzed by means of chi-square (or Fisher's exact test when needed). To examine adjusted predictors of complications, variables that were considered clinically relevant and that showed an univariate relationship with outcome were entered into a logistic regression model. Variables for inclusions were carefully chosen, given the number of events available, to avoid overfitting of the final model. Goodness-of-fit (Hosmer-Lemeshow) test was reported. The correlation between platelets (PTL) minimum and time length of IABP implantation was investigated by means of a linear regression analysis (Pearson's *r* value). A receiver operating characteristic (ROC) curve was plotted to identify a cutoff of nadir PTL count with respect to complications. A 2-tailed *P* value less than 5% was considered statistically significant.

## Results

Baseline data of the study group are shown in Table 1. The mean age of patients in the study was  $69.6 \pm 12.3$  years;

Table 1. Baseline Demographics and Clinical Characteristics of the 481 Patients Included in the Study

	Mean $\pm$ SD or Frequency (%)
Age (y)	69.6 $\pm$ 12.3
Gender (M/F)	333/148 (69.2/30.8)
BSA (m <sup>2</sup> )	1.85 $\pm$ 0.19
Familiar history	121 (25.2)
Smoke habit (ever smokers)	251 (52.2)
Obesity	92 (19.1)
Hypertension	249 (51.8)
Dyslipidemia	153 (31.8)
Diabetes	108 (22.5)
Peripheral arteriopathy	17 (3.4)
Neurologic impairment	16 (3.2)
Previous myocardial infarction	120 (24.9)
Previous PCI	102 (21.2)
Previous cardiac surgery	12 (2.5)
Chronic renal disease	42 (8.7)
Chronic obstructive pulmonary disease	44 (9.1)
Neoplasm	36 (7.5)
Abbreviations: BSA, body surface area; PCI, percutaneous coronary intervention; SD, standard deviation.	

69.2% were men. Hypertension was detectable in 51.8% ( $n = 249$ ), dyslipidemia in 31.8% ( $n = 153$ ), and diabetes mellitus in 22.5% ( $n = 108$ ). About one-fourth of patients (24.9%) showed prior myocardial infarction and the 21.2% of patients had a prior PCI.

Indications to IABP implantation are depicted in Table 2.

In our population, IABP was positioned for ST-elevation myocardial infarction (STEMI) in most cases (70.1%). Among STEMI patients, IABP was implanted in patients in Killip class I/II (31.4%) because of LIRA and in 35.3% of patients because of cardiogenic shock. In unstable angina or non-ST-elevation myocardial infarction (NSTEMI) the most common indications were severe coronary artery disease in high-risk patients (29.2%), followed by persistent hypotension (17.5%), cardiogenic shock (15.8%), and periprocedural complications (10.8%). IABP was positioned in 10 patients (8.3%) with CABG indication for presurgery stabilization.

Devices and therapies used during hospitalization are showed in Table 3. In the majority of patients (66.1%,  $n = 318$ ) IABP was the only device, while in the remaining (33.9%) it was associated with other devices. The device most frequently associated with IABP was mechanical ventilation (44.7%; invasive: 26.0%; noninvasive 18.7%). The continuous venovenous renal replacement therapy was used in the 14.8% ( $n = 71$ ) of patients. Unfractionated heparin was used in 95.8% of patients. The majority of patients

Table 2. IABP Indications

Diagnosis	IABP Indication	Frequency (%)
STEMI (n = 337 [70.1%])	Large ischemic risk area	106 (31.4)
	Cardiogenic shock	119 (35.3)
	Hypotension	45 (13.4)
	Sudden death/VF	15 (4.4)
	In the catheter laboratory	4
	Outside the catheter laboratory	11
	PCI failure	14 (4.2)
	Acute pulmonary edema	14 (4.2)
	Mechanical complications	19 (5.6)
	Mitral regurgitation	9
UA/NSTEMI (n = 120 [24.9%])	VSD	10
	Periprocedural complications	2 (0.6)
	Preoperative support	3 (0.9)
	Severe coronary artery disease in high risk patients	35 (29.2)
	Hypotension	21 (17.5)
	Cardiogenic shock	19 (15.8)
	Periprocedural complications	13 (10.8)
	Acute pulmonary edema	10 (8.3)
	Preoperative support	10 (8.3)
	Sudden death/VF	8 (6.6)
CHD with CABG indication (n = 9 [1.9%])	In the catheter laboratory	4
	Outside the catheter laboratory	4
	Mechanical complications	2 (1.7%)
	Mitral regurgitation	2
	VSD	0
	PCI failure	2 (1.7%)
	Preoperative support	9 (100%)
	Election procedure	1 (6.7%)
	Cardiogenic shock	14 (93.3%)

Abbreviations: CABG, coronary artery bypass graft; CHD, coronary heart disease; IABP, intraaortic balloon pump; NSTEMI, non-ST elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST elevation myocardial infarction; UA, unstable angina; VF, ventricular fibrillation; VSD, ventricular septal defect.

received dual antiplatelet therapy: acetylsalicylic acid (90.0%) and clopidogrel (81.7%). Therapy with glycoprotein IIb/IIIa inhibitors was administered in 55.1% of cases. Inotropic agents (epinephrine, norepinephrine, dopamine,

Table 3. Devices and Drugs

	Frequency (%)
Devices	
IABP only	318 (66.1)
IABP + 1 other device	70 (14.6)
IABP + 2 other devices	64 (13.3)
IABP + 3 other devices	29 (6.0)
IABP	481 (100)
IOT	124 (26.0)
C-PAP	90 (18.7)
CVVHDF	71 (14.8)
Drugs	
Unfractionated heparin	461 (95.8)
Acetylsalicylic acid	433 (90.0)
Clopidogrel	393 (81.7)
Glycoprotein IIb/IIIa inhibitors	265 (55.1)
Inotropes	214 (44.5)
Ticlopidin	15 (3.1)

Abbreviations: C-PAP, continuous positive airways pressure ventilation; CVVHDF, continuous venovenous hemodiafiltration; IABP, intraaortic balloon pump; IOT, orotracheal intubation.

Table 4. IABP Complications

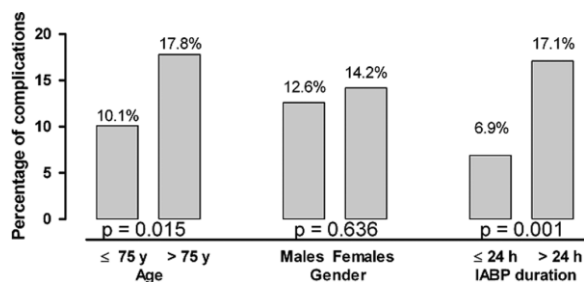
	Frequency (%)
Complications (total)	63/481 (13.1)
Strictly related to IABP	
Severe bleeding	33 (52.4)
Nonspecific site (acute anemia)	16 (58.5)
Bleeding at the insertion site	13 (39.4)
Retroperitoneal hematoma	4 (12.1)
Limb ischemia	10 (15.9)
Systemic embolization (renal/mesenteric infarct)	5 (7.9)
Pseudoaneurysm of femoral artery	3 (4.8)
Not strictly related to IABP	
Gastrointestinal and urinary bleeding	12 (19.0)

IABP, intraaortic balloon pump.

and dobutamine) were used in 44.5% of patients, all with cardiogenic shock.

### Complications

Data regarding complications are shown in Table 4. In our series, complications were observed in 13.1% (63/481) of patients. Thirty-three patients (out of 63, 52.4%) showed



**Figure 1.** Incidence of IABP complications. Abbreviation: IABP, intraaortic balloon pump.

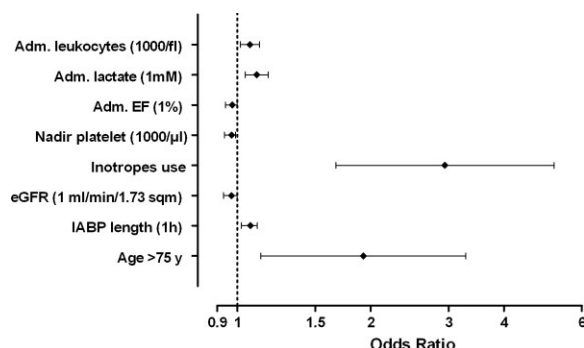
major bleeding, among whom one-half exhibited unknown bleeding site while bleeding at the insertion site occurred in 13 patients. Four patients developed a retroperitoneal hematoma (1 patient died). Limb ischemia complicated hospital course in 10 patients, all reversed by IABP removal. The less frequent adverse events in our series were the occurrence of renal infarct (2 patients) and mesenteric infarct (3 patients) caused by systemic embolization. Three patients developed pseudoaneurysm of femoral artery at the IABP insertion site.

Twelve patients (19.0%) developed complications not strictly related to IABP implantation, represented by severe gastrointestinal or urinary bleeding.

As depicted in Figure 1, the incidence of complications was higher in patients aged >75 years ( $P = 0.015$ ) and in those who had a IABP implanted for more than 24 hours ( $P = 0.001$ ) whereas no difference was observed between males and females in the incidence of complications. In the overall population, median time length of IABP treatment was 36 hours (25th–75th percentile: 22–50 hours).

**Predictors of Complications:** Unadjusted predictors of complications at univariable logistic regression analysis are depicted in Figure 2.

At multivariable logistic regression analysis the following variables resulted independent predictors for complications (when adjusted for age >75 years, estimated glomerular filtration rate [eGFR], and time length of IABP support): inotropes drug use (yes vs no) (OR 2.450; 95% CI, 1.168–5.035;  $P = 0.017$ ); nadir platelet count (1000/ $\mu$ l step) (OR 0.990; 95% CI, 0.985–0.996;  $P < 0.001$ );



**Figure 2.** Unadjusted predictors of complications at univariable logistic regression analysis. Abbreviations: EF, ejection fraction; eGFR, estimated glomerular filtration rate; IABP, intraaortic balloon pump.

Admission lactate (1 mmol per 1 step) (OR 1.175; 95% CI, 1.058–1.306;  $P = 0.003$ ). Hosmer and Lemeshow goodness-of-fit test  $\chi^2 = 9.61$ ,  $P = 0.294$ .

At linear regression analysis, nadir PTL count showed a negative correlation with time length of IABP implantation ( $r = -0.31$ ;  $P < 0.001$ ). A cutoff value of less than 120,000 for nadir PTL count was identified on a ROC curve for the development of complications (area under the curve [AUC] 0.70; 95% CI, 0.63–0.68;  $P < 0.001$ ); sensitivity 65%, specificity 72%; predictive value of positive test 27%, predictive value of negative test 92%. In facts, patients with nadir PTL less than 120,000/ $\mu$ L showed a higher complication rate (26.7 vs 7.3%,  $P < 0.001$ ), with an OR 4.617 (95% CI, 2.645–8.064). A median time length of IABP treatment of 45.5 hours was identified on a ROC curve for the development of nadir platelet count (AUC 0.68; 95% CI, 0.63–0.73;  $P < 0.001$ ); sensitivity 63%, specificity 65%; predictive value of positive test 46%, predictive value of negative test 78%.

In our series, 2 patients developed HIT and were treated with lepirudin; 1 patient died because of retroperitoneal hematoma.

### Mortality

In our population, 100 patients died (100/481; 20.8%). Among patients who died, IABP was implanted due to cardiogenic shock or persistent hypotension in 75 patients (75%); cardiac arrest in 8 patients (8%); periprocedural complications of PCI in 6 patients (6%); mechanical complication of acute myocardial infarction in 4 patients (4%); LIRA in 4 patients (4%); acute pulmonary edema in 2 patients (2%); and bridge to CABG in 1 patient (1%). Patients who developed complications showed an in-ICCU mortality significantly higher than patients who did not (44.4% vs 17.2%;  $P < 0.001$ ).

### Discussion

The main finding of our investigation, which was performed in a large series of patients treated with IABP, is that the degree of hemodynamic impairment (as indicated by inotropes use and admission lactate) and the nadir platelet count are independent predictors of complications, whose development was associated with a higher in-ICCU mortality.

The development of thrombocytopenia after IABP implantation has been investigated in previous studies,<sup>8,12–15</sup> with conflicting results. In 1978, McCabe et al<sup>12</sup> reported that thrombocytopenia, though detectable in all patients, was not related to the development of complications. Vonderheide et al<sup>13</sup> observed, in a prospective study of 58 patients treated with IABP, that the use of this device led to steady and predictable decrease in platelet count, which recovered rapidly if the balloon pump was removed or slowly if the device remained in place. Bream-Rouwenhorst et al,<sup>14</sup> in a retrospective cohort study involving 107 patients undergoing IABP, reported that the development of thrombocytopenia occurred in 58% of patients and was not related to the use of antiplatelet therapy. Recently, Roy et al<sup>8</sup> assessed the incidence and predictors of thrombocytopenia in 252 consecutive patients treated with IABP and documented



that in-hospital death and major bleedings were higher in patients who developed thrombocytopenia. However, since at multivariable analysis thrombocytopenia was not an independent predictor either of in-hospital death or major bleeding, the authors concluded that IABP-associated thrombocytopenia should not necessarily prompt discontinuation of IABP support or important adjunctive medications. Similarly, in a recent small observational study,<sup>15</sup> thrombocytopenia, though a common finding, was not associated with serious adverse consequences.

Since the development of IABP in 1962,<sup>16</sup> the incidence rate and the type of complications have deeply changed over time. Whereas in 1978, McCabe et al.<sup>12</sup> reported an incidence rate of 23% and complications were mainly represented by vascular damage induced by insertion, in the Benchmark Registry<sup>17</sup> (enrolling 16,909 patients), complication rate dropped to 2.6% and major bleeding and limb ischemia were the most frequent complications.

Whereas progress in IABP technology can account for the significant reduction in vascular complications, nowadays major bleedings remain the most frequent complications in patients treated with IABP support and still represent a clinical and therapeutic challenge.

In our study, performed in a larger series of patients, we confirmed that major bleedings are the most frequent complications and documented that the nadir platelet count is an independent predictor of complications and that thrombocytopenia can be related to mechanical factors because it is inversely correlated to the duration of IABP support.

In our series, unfractionated heparin was administered to nearly all patients (95.8%) and heparin-related immunogenic and nonimmunogenic causes of thrombocytopenia, when suspected, have been excluded by means of testing for HIT. The inverse relation between thrombocytopenia and IABP duration strongly suggests that the reduction in PTL can be related to mechanical factors.

Recent reports<sup>18,19</sup> strongly suggest a relation between baseline or acquired thrombocytopenia and outcomes (ischemic and hemorrhagic complications) was suggested in patients undergoing PCI for acute coronary syndrome. In an analysis of the HORIZONS-AMI trial, baseline thrombocytopenia in STEMI patients was associated with early adverse events, related to both ischemia and bleeding.<sup>18</sup> In the ACUTY trial, acquired thrombocytopenia, occurring in approximately 1 in 14 patients, was strongly associated with hemorrhagic and ischemic complications.<sup>19</sup>

## Conclusion

In conclusion, in consecutive patients treated with IABP support, the development of complications is associated with higher in-ICCU mortality. The degree of hemodynamic impairment (as indicated by inotropic use and admission lactate) and the nadir platelet count (whose development is related to the duration of IABP support) were independent predictors of complications.

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